REMARKS

Status of Claims

Claims 1-4 and 10 have been amended.

Claims 6-9 and 11-15 have been canceled.

Claims 16-20 have been added.

Claims 1-5, 10 and 16-20 are now pending for the Examiner's consideration.

Amendments to the Claims:

Applicant has added Claims 16-20.

Support for new Claim 16 can be found, for example, in Calim 5 and in Example 6 of the originally-filed specification.

Support for new Claims 17-20 can be found, for example, in the originally-filed specification at page 4, lines 5-13.

No new matter is added by the way of these amendments.

Applicant respectfully requests reconsideration and withdrawal of the outstanding rejections, in light of the foregoing amendments and following remarks.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-4 were rejected under 35 U.S.C. § 112, second paragraph, for the reasons set forth on page 2 of the Office Action. By the present amendments, Applicant believes the rejection has been overcome, and respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 1 was rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully disagree with this allegation for the following reasons.

Claim 1 is directed to a method for treating cancer in a patient in need of such treatment, the method comprising administering to the patient a combination of a therapeutically effective amount of *N*-[(R)-2,3-dihydroxy-propoxy]-3,4-difluro-2-(2-fluoro-4-iodo-phenylamino)-benzamide and a therapeutically effective amount of capecitabine.

The present application teaches simultaneous therapy with capecitabine and *N*-[(R)-2,3-dihydroxy-propoxy]-3,4-difluro-2-(2-fluoro-4-iodo-phenylamino)-benzamide or PD325901 as follows:

"This experiment examined simultaneous therapy with capecitabine and PD325901 both given on days 17-30. Many of the combination regimens in this experiment were toxic. Only three combination regimens could be evaluated for efficacy. One of these, 6.25 mg/kg Compound A and 650 mg/kg capecitabine produced 100% complete regressions, a net cell kill value of 1.9 logs, and 40% tumor free survivors on day 129. **This is significantly superior activity compared to either of the single agents at their MTDs.**" Example 6; emphasis added.

Given these findings and the facts that *N*-[(R)-2,3-dihydroxy-propoxy]-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-benzamide, also known as PD 0325901, is in an ongoing Phase 2 clinical study in patients with breast, colon, nonsmall cell lung cancer (NSCLC) or melanoma and capecitabine is converted by the body to 5-fluorouracil (5-FU), a drug which has been given intravenously for many years to treat various types of cancer, one with ordinary skill in the art is able to practice the claimed invention.

Accordingly, Applicant respectfully requests that the rejection be withdrawn.

Rejection under 35 U.S.C. § 103

Claims 1-10 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over McKearn et al., U.S. 6,858,598 in view of Barnett et al., US2004/0102360 A1 and Coleman et al., US 2005/0234080 A1 for the reasons set forth on pages 5-7 of the Office Action.

In light of cancellation of Claims 6-10, this rejection is moot with regard to these claims.

Further, Applicant believes the rejection is not applicable to the pending claims for the following reasons.

McKearn et al. is limited to a method of using a matrix ***metalloproteinase*** (MMP) inhibitor and optionally radiation therapy, and one or more antineoplastic agents of the topoisomerase class selected from the group consisting of irinotecan and topotecan, as a combination therapy for the treatment of neoplasia. **Matrix metalloproteinases** (MMPs) are zinc-dependent endopeptidases; capable of degrading all kinds of extracellular matrix proteins. Nowhere McKearn et al. teaches ***signaling kinases*** MEK1 and MEK2 (MEK 1/2) which are dual-specificity kinases that activate the ERK family kinases, ERK1 and ERK2, by phosphorylation of both threonine and thyrosine. Accordingly, McKearn et al. is irrelevant for the subject matter of the present invention.

Barnett et al. does not cure the deficiencies of McKearn et al. In paragraph [0070] to which the Office Action refers, Barnett et al. merely states that "Another aspect of this invention is that the protein kinase, including serine-threonine protein kinase, whose catalytic activity is inhibited by a compound utilized in the method of treatment of this invention, is selected from the group consisting of but not limited to CDK2, Raf, Mek, p38, Erk, JNK, and mTOR" and does not indicate any type of MEK inhibitors. In paragraph [0118] Barnett et al. just lists capecitabine among many other antiproliferative agents as follows: "Antiproliferative agents" includes antisense RNA and DNA oligonucleotides such as G3139, ODN698, RVASKRAS, GEM231, and INX3001, and antimetabolites such as enocitabine, carmofur, tegafur, pentostatin, doxifluridine, trimetrexate, fludarabine, capecitabine, galocitabine, cytarabine ocfosfate, fosteabine sodium hydrate, raltitrexed, paltitrexid, emitefur, tiazofurin, decitabine, nolatrexed, pemetrexed, nelzarabine, 2'-deoxy-2'-methylidenecytidine, 2'-fluoromethylene-2'-deoxy- cytidine, N-[5-(2,3-dihydro-benzofuryl)sulfonyl]-N'-(3,4-dichlorophenyl)ur- ea, N6-[4-deoxy-4-[N2-[2(E),4(E)-tetradecadienoyl]glycylamino]-L-glycero-B- -L-manno-heptopyranosyl]adenine, aplidine,

ecteinascidin, troxacitabine, 4-[2-amino-4-oxo-4,6,7,8-tetrahydro-3H-pyrimidino[5,4-b][1,4]thiazin-6-yl- -(S)-ethyl]-2,5-thienoyl-L-glutamic acid, aminopterin, 5-flurouracil, alanosine, 11-acetyl-8-(carbamoyloxymethyl)-4-formyl-6-methoxy-14-oxa-1,1- 1-diazatetracyclo(7.4.1.0.0)-tetradeca-2,4,6-trien-9-yl acetic acid ester, swainsonine, lometrexol, dexrazoxane, methioninase, 2'-cyano-2'-deoxy-N-4-palmitoyl-1-B-D-arabino furanosyl cytosine, 3-aminopyridine-2-carboxaldehyde thiosemicarbazone and trastuzumab." Furthermore, Barnett et al. teaches away from the present invention because Barnett et al. is limited to methods of treating cancer using a specific combination of at least two Akt inhibitors or a compound which is an inhibitor of Akt and an inhibitor of a protein kinase. Akt (protein kinase B) is a serine/threonine kinase, which activation involves growth factor binding to a receptor tyrosine kinase and activation of PI 3-K, which phosphorylates membrane bound PIP_2 to generate PIP_3.

Likewise, Coleman et al. does not cure the deficiencies of both McKeam et al. and Barnett et al. Without any reference to the combination of the present invention, Coleman et al. merely states that in paragraph [0383] that "Inhibitors of cell proliferation and survival signalling pathway" refer to compounds that inhibit signal transduction cascades downstream of cell surface receptors. Such agents include inhibitors of serine/threonine kinases (including but not limited to inhibitors of Akt such as described in WO 02/083064, WO 02/083139, WO 02/083140 and WO 02/083138), inhibitors of Raf kinase (for example BAY-43-9006), inhibitors of MEK (for example CI-1040 and PD-098059), inhibitors of mTOR (for example Wyeth CCI-779), and inhibitors of PI3K (for example LY294002)." Furthermore, Coleman et al. teaches away from the present invention because Coleman et al. is specifically limited to dihydropyrimidone compounds that are useful for treating cellular proliferative diseases, for treating disorders associated with KSP kinesin activity, and for inhibiting KSP kinesin.

Accordingly, Applicant respectfully requests that the rejection under § 103 be withdrawn.

Claims 11-15 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Barrett et al., US 6,960,614 B2 in view of Coleman et al., US 2005/0234080 A1 and Barnett et al., US2004/0102360 A1, and further in view of McKeam et al., U.S. 6,858,598 for the reasons set forth on pages 7-8 of the Office Action.

In light of cancellation of Claims 11-15, the rejection is moot.

Conclusion

Applicant believes all claims are now in condition for allowance. Should there be any issues that have not been addressed to the Examiner's satisfaction, Applicant invites the Examiner to contact the undersigned attorney.

Applicant does not believe any fees are due in connection with this response. If any fees are due in connection with this response, please charge such fees to Deposit Account No. 500329.

Respectfully submitted,

Date: May 10, 2006

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